
Article:
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Excess mortality associated with eating disorders: a population-based cohort study.

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Abstract:	Background Individuals with eating disorders (EDs) have a high mortality risk. Few population-based studies have estimated mortality risk in EDs other than anorexia nervosa. Aims To investigate all-cause mortality within a population-based cohort of individuals who received hospital-based care for any ED (anorexia nervosa, bulimia nervosa or ED not otherwise specified) in Ontario, Canada. Methods We conducted a retrospective-cohort study of 19,041 individuals with an ED from January 1, 1990, to December 31, 2013 using administrative healthcare data. The outcome of interest was death. Excess mortality was assessed using standardized mortality ratios (SMRs) and potential years of life lost (PYLL). Cox proportional hazards regression models were used to examine socio-demographic and medical comorbidities associated with greater mortality risk. Results The ED cohort had 17,108 females (89.9%) and 1,933 males (10.1%). The all-cause mortality for the entire ED cohort was five times higher than expected compared to the Ontario population (SMR = 5.06; 95% CI:4.82-5.30). SMRs were higher for males (SMR=7.24; 95% CI: 6.58-7.96) relative to females (SMR=4.59; 95% CI: 4.34-4.85), overall and in all age groups in the cohort. For both sexes, the ED cohort PYLL was more than 6 times higher than the expected PYLL in the Ontario population.

	Conclusions and Relevance Patients with EDs experience five to seven times higher mortality rates compared to the overall population. There is an urgent need to understand the mortality risk factors to improve health outcomes among individuals with eating disorders.

Excess mortality associated with eating disorders: a population-based cohort study

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KEY POINTS

Question: What is the mortality rate for individuals with eating disorders?

Findings: This study of 19,041 individuals with eating disorders found that eating disorders are associated with an elevated risk of premature of death. The all-cause mortality for the entire cohort was five times higher than expected compared to the general population. Standardised mortality ratios were higher overall for males (SMR = 7.24) relative to females (SMR = 4.59).

Meaning: Individuals with eating disorders experience excess premature mortality compared to the general population. These findings highlight the need to develop focused interventions for this group to improve health outcomes.

ABSTRACT

Background

Individuals with eating disorders (EDs) have a high mortality risk. Few population-based studies have estimated mortality risk in EDs other than anorexia nervosa.

Aims

To investigate all-cause mortality within a population-based cohort of individuals who received hospital-based care for any ED (anorexia nervosa, bulimia nervosa or ED not otherwise specified) in Ontario, Canada.

Methods

We conducted a retrospective-cohort study of 19,041 individuals with an ED from January 1, 1990, to December 31, 2013 using administrative healthcare data. The outcome of interest was death. Excess mortality was assessed using standardized mortality ratios (SMRs) and potential years of life lost (PYLL). Cox proportional hazards regression models were used to examine socio-demographic and medical comorbidities associated with greater mortality risk.

Results

The ED cohort had 17,108 females (89.9%) and 1,933 males (10.1%). The all-cause mortality for the entire ED cohort was five times higher than expected compared to the Ontario population (SMR = 5.06; 95% CI:4.82-5.30). SMRs were higher for males (SMR=7.24; 95% CI: 6.58-7.96) relative to females (SMR=4.59; 95% CI: 4.34-4.85) overall, and in all age groups in the cohort. For both sexes, the ED cohort PYLL was more than 6 times higher than the expected PYLL in the Ontario population.

Conclusions and Relevance

Patients with EDs experience five to seven times higher mortality rates compared to the overall population. There is an urgent need to understand the mortality risk factors to improve health outcomes among individuals with eating disorders.

Declaration of Interest

None.

Keywords:

Eating disorders; anorexia nervosa; bulimia nervosa; EDNOS; mortality; standardized mortality ratio; male; female

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Relevance Statement

Eating disorders, including anorexia nervosa, bulimia nervosa, and eating disorders not otherwise specified, are associated with high illness burden, including mortality. This study uses population-based data to estimate standardized mortality ratios (SMRs) comparing the rate of mortality amongst individuals with eating disorders to the general population in Ontario, Canada. The SMR for individuals with eating disorders was 5.06, reflecting a 5-fold increase in mortality risk for individuals with eating disorders. For males, the risk was 7-fold higher (SMR - 7.24). Understanding the risk factors for the increased mortality in eating disorders is critical to reduce mortality in this clinical population.

INTRODUCTION

Eating disorders are associated with a high risk of mortality and high illness burden including major depression, post-traumatic stress disorder, and chronic conditions including cardiovascular, heart failure, musculoskeletal and renal complications as observed in clinical population samples. (1-4) One meta-analysis reported an overall elevated mortality rate for eating disorders (anorexia nervosa, bulimia nervosa, and eating disorder not otherwise specified), which in some instances was much higher than other psychiatric disorders. (5) Eating disorders have also been associated with high health care costs, related to both psychiatric and non-psychiatric hospitalizations. Previous research has found that direct health care costs for individuals hospitalised for an eating disorder were about $48 million, with higher costs for those under the age of 20 and those 65 and older. (1) However, few population-based surveillance studies estimating incidence, prevalence and mortality in eating disorders have been published (2, 6, 7), with the literature on the epidemiology and outcomes of eating disorders having significant limitations such as small sample sizes and few large-scale mental health surveillance studies.(2, 6)

Most of the literature reporting on mortality in eating disorder patients comes from studies examining cohorts in specific treatment settings, which are difficult to compare given the wide variability in treatment target populations, insurance coverage and other selection biases. (8, 9) Several mortality studies report only crude case fatality rates (i.e., they report on deaths among patients with no comparison group or adjustment for expected mortality in the same age population); other studies are limited in sample size or scope and report only on anorexia nervosa and/or only examine female patients.(9, 10) Eating disorders have been misperceived as rare perhaps due to limited awareness of the available data on the burden of disease or a misconception that only the most

severe cases experience a severe burden. (11, 12) Furthermore, the lack of comprehensive data on eating disorders that includes both males and females has made it difficult to estimate all-cause and cause-specific mortality among this population.

This study describes all-cause mortality rates within a population-based cohort of patients with an eating disorder in a context of universal public health care funding. Excess mortality among these patients was estimated relative to the general population without an eating disorder using standardized mortality ratios (SMRs) and potential years of life lost (PYLL) (in total and attributable to eating disorders). In addition, factors associated with increased hazard of mortality within the ED cohort were examined including patient socio-demographic and comorbidity measures as well as indicators of health care service utilization.

METHODS

Study design

This study examines a population-based, retrospective cohort of individuals who received care for an eating disorder in any hospital in Ontario from January 1, 1990, to December 31, 2013. The cohort was followed, through record-linkage, until date of death or December 31, 2013, the latest date possible based on data availability at the time of the analysis).

Data sources

We made use of administrative health care data available through ICES in Toronto, Ontario. ICES is an independent non-profit organization funded by the Ontario Ministry of Health and holds an inventory of coded and linkable health datasets, encompassing much of the publicly funded administrative health services records for the Ontario population eligible for universal health coverage

since 1986. This data repository includes individual-level, linkable longitudinal data on most publicly funded health care services. The Registered Persons Database (RPDB), a population-based registry, contains anonymized demographic data on all insured members of the universal Ontario Health Insurance Plan (OHIP), such as sex, date of birth, urban or rural dwelling information and neighbourhood-level income (measured in quintiles at the census tract level). Information on date and cause of death (where applicable) were obtained from the Ontario Registry General-Death Vital Statistics. Hospital admissions and associated diagnostic codes used to define the cohort were obtained from the following health care administrative databases maintained by the Canadian Institute for Health Information: Discharge Abstract Database (DAD) for non-mental health admissions and National Ambulatory Care Reporting System (NACRS) for emergency department visits. Psychiatric hospitalization records were obtained from the Ontario Mental Health Reporting System (OMHRS) database.

Co-morbidity data for chronic medical conditions were obtained via the following validated patient cohorts and registries developed, linked and analyzed at ICES including: Ontario Congestive Heart Failure (CHF) Database; Chronic Obstructive Pulmonary Disease (COPD) Database; Ontario Diabetes Database (ODD); Ontario Asthma Database; Ontario HIV Database and Ontario Cancer Registry (OCR). These datasets have been described elsewhere. (13)

Derivation of the eating disorder patient cohort

Individuals were included if they received an eating disorder diagnosis during an emergency department visit, medical hospitalization, or psychiatric hospitalization from 1990 to 2013. The first diagnosis from any of these data sources was determined as the cohort entry date. Cohort development and analyses were carried out with linked administrative health care data holdings at

ICES. Diagnostic codes used to identify eating disorder patients included: ICD-9 codes 307.1 (anorexia nervosa), 307.51 (bulimia nervosa), 307.50 (eating disorders not otherwise specified); ICD-10 codes F50.0 (eating disorders), F50.1 (anorexia nervosa), F50.2, F50.3 (bulimia nervosa), F50.8, F50.9 (EDNOS), and DSM-IV codes 307.1 (anorexia nervosa), 307.51 (bulimia nervosa), 307.50 (EDNOS). We restricted our study to these three ED diagnoses because the publicly-funded services in Ontario focus on the treatment of these ED diagnoses. ED diagnosis codes do not apply to children under the age of 5. Furthermore, children ages 5 to 9 were excluded as the small number of deaths precluded reporting under Ontario privacy regulations. We excluded individuals who ceased to be publicly insured for health care at date of cohort entry. This approach resulted in a cohort of 19,041 individuals with and eating disorder diagnosis (including all patients deceased or alive to the end of December 31, 2013).

The development of this cohort, restricted to individuals alive as of January 1,2014, has also been described elsewhere. (14)

Analysis

Mortality rates were estimated for the full cohort and were reported as deaths per 1,000 person-years of observation time, overall and by sex (female and male), calendar year (from 1990 to 2013), and age groups. Person-years of follow-up were segregated by sex, calendar year and age attained over follow-up (to end of follow-up, or death) for each cohort member. This was achieved using Lexis expansion tools for cohort data using Stata 14 (StataCorp. 2015. *Stata Statistical Software: Release 14*. College Station, TX: StataCorp LP). Excess mortality in the eating disorder population, relative to the underlying Ontario population, was illustrated in several ways including SMRs, PYLL in the cohort, and proportion of PYLL attributable to eating disorder.

SMRs were estimated using the indirect method.(15) SMRs were defined as the number of observed deaths in the eating disorder cohort divided by the number of expected deaths in the cohort if the eating disorder cohort had had the same sex- and age-specific mortality experience as the underlying Ontario population. Expected mortality rates in the general population were obtained using all Ontario deaths in 2011 and corresponding data for the 2011 Census year. SMRs were presented with exact Poisson-based 95% confidence intervals.

Person Years of Life Lost (PYLL) within the eating disorder cohort were estimated as the sum of all years of life lost before age 75 (16) for observed deaths among patients with an eating disorder (expressed as PYLL per 1,000 persons). Expected and excess (eating disorder attributable) PYLL values were also estimated using expected deaths from Ontario 2011 standard mortality rates. The theoretical percent of total PYLL attributable to being in the eating disorder cohort (relative to the underlying population) was defined as attributable PYLL = (total cohort PYLL – expected PYLL)/ total cohort PYLL and expressed as a percentage.

Socio-demographic factors associated with higher risk of mortality within the cohort were examined using Cox Proportional Hazard regression models for all-cause mortality. Patients who entered the cohort with an eating disorder diagnosis on the same day as death contributed no follow-up time and were excluded from the survival models (N=5). Separate Cox models were estimated for patients aged 10 to 44 at entry and those 45 and older. Patient socio-demographic characteristics considered were age, sex and calendar year over the period of the study, as well as neighbourhood-level household income quintile and rurality of residence. Models examining the effect of socio-demographic variables were then further adjusted for medical co-morbidity (i.e., chronic conditions,

defined beforehand). The adjusted models included six chronic conditions derived from validated cohorts through administrative databases.

Model diagnostics were performed and indicated no violations of assumptions. This included confirmation of the validity of a linear effect of age as a continuous covariate in the exponential Cox model, assessment for non-violation of the assumption of proportional hazards, and lack of excess multi-collinearity.

Ethics and approvals

ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. Thus, the use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. The project was approved by the Research Ethics Board at University Health Network, Toronto.

RESULTS

Baseline characteristics of the eating disorder cohort are presented in Table 1. Of the 19,041 cohort members, 17,108 were female (89.9%) and 1,933 were male (10.1%). Age at cohort entry ranged from 10 to over 85 years of age, but 88.9% of the population entered the cohort between the ages of 14 and 44. Most of the cohort (88.8%) resided in urban centres. A greater percentage of the cohort lived in middle to low-income neighbourhoods, with 37.4% in the lowest neighbourhood level income category and 18.0% in the middle-income neighbourhood level income category. Categories for eating disorder-specific diagnoses at cohort entry revealed multiple diagnoses for the same individual over time; 31.8% of the cohort had anorexia nervosa alone or in combination with bulimia nervosa and/or eating disorder not otherwise specified (EDNOS); 35.1% of the cohort had a diagnosis of EDNOS alone at enrolment. Eating disorder diagnoses were also comorbid with other medical conditions including asthma (27.0%), diabetes (8.9%), cancer (4.6%) and congestive heart failure (3.5%).

Table 2 presents descriptive statistics for the mortality follow-up analysis of this cohort, including total person-years of follow up and observed deaths, for the whole cohort and by age group and sex. Mortality rates and SMRs by age group and sex are also presented in Table 2. For the entire eating disorder cohort and across all age groups, the all-cause mortality rate was five times higher than expected based on mortality rates in the Ontario population (marginal SMR = 5.06; 95% CI:4.82-5.30). Peak values for SMRs were observed among adults from approximately 30 to 44 years of age. Mortality rates and SMRs were unstable for individuals 10 to 14 due to small number of deaths. SMRs were higher for male eating disorder patients, relative to female, overall and in all age groups. For females, the marginal SMR was 4.59 (95% CI: 4.34-4.85) while for males it was 7.24 (95% CI: 6.58-7.96).

Excess mortality is further illustrated in Figure 1, which presents cohort and population mortality rates (per 1,000 population) by age and sex as well as age-sex specific SMRs.

The overall expected PYLL (based on expected numbers of deaths in the cohort using the 2011 Ontario age-specific death rates) was estimated at 29.54 years per 1,000 population (95% CI: 28.7-30.4) and similar for each sex separately (Appendix Table 1). Within the eating disorder cohort, estimated total PYLL before age 75 equalled 191.6 per 1,000 population (95% CI: 189.4-193.8), for both sexes, combined. Years of life lost per 1,000 population was higher for males (PYLL within cohort=375.6; 95% CI: 364.7-386.8) relative to females (PYLL within cohort=174.1; 95% CI: 171.9-176.3). For both sexes, the excess PYLL attributable to experiencing an eating disorder was 84%. For female eating disorder patients, it was estimated that 83% of PYLL were attributable to being in the eating disorder cohort; for male eating disorder patients, this value was 92%. Among all Ontario ED patients, over the period of this study, it was estimated that 24,773 years of life were lost due to eating disorder, before the age of 75.

Cox survival models on all-cause mortality, controlling for the effects of demographic characteristics, appear in Table 3. For both age groups (10-44 and >=45 years of age), older age (as a continuous, linear term) and male sex were associated with statistically significant increased mortality risk and adjusted hazard ratio of 1.91 in both age groups. Additionally, mortality declined over calendar years in the analysis showing a statistically significant effect of calendar year on the downward trend in mortality over time (adjusted hazard ratio of 0.9, year over year). In addition, the pattern of association with household income quintile was not a simple linear association, but rather a U-shaped pattern. Higher total mortality hazard ratios were observed in the highest and lowest income quintiles, relative to household income quintiles in the middle.

Fully adjusted models for age, sex and calendar year resulted in opposite findings for rurality in the analyses for cohort members under and over 45 years of age. Rural residence was associated with lower mortality for cohort members under the age of 45 but higher mortality risk for cohort members 45 or older. Control variables for non-ED chronic medical conditions (CHF, COPD, cancer and HIV) were all positively associated with higher mortality ratios with the exceptions of inverse associations for asthma and diabetes diagnoses within cohort members age 45 and over. For cohort members ages 44 and younger, having a diagnosis of CHF, cancer, diabetes and HIV was positively associated with higher mortality ratios. We observed a simple linear trend toward lower mortality with calendar year of entry into the cohort. This cannot be separated from a general trend in improved survival in the population as age-sex specific mortality risk expected in the population are not updated for each calendar year but based on census years (here based on the 2011 Canadian census).

DISCUSSION

The purpose of this study was to estimate the excess mortality and burden associated with eating disorders using comprehensive population-based data. Notably, this study is among the few internationally that have made use of a population-based eating disorder cohort and to have provided SMR estimates specific to both female and male patients. Our findings show that individuals with eating disorders diagnosed in hospital settings had a mortality rate of approximately 5-fold higher than the general population, with more than 80% of life lost before the age of 75 for females and males.

In female eating disorder patients, we found a roughly five-fold mortality rate relative to the general population. This is similar in magnitude to what has been reported in two international meta-analyses (5, 8) and similar in magnitude to SMRs reported specifically for anorexia nervosa (anorexia

nervosa being the eating disorder diagnosis with the highest SMRs). Whilst studies have reported on the lifetime prevalence of eating disorders in males ranging from 0.1 to 2.0 for all types,(2, 9) few studies have reported on the mortality rates among males with eating disorders and those studies tend to report exclusively on anorexia nervosa.(17, 18) Our study thus makes a novel and important contribution to the sparse literature on male eating disorder patients and their mortality experience, with a substantially larger sample of male eating disorder patients.

The SMRs observed in males were almost 2-fold higher than in females. This observation of higher mortality in males with eating disorders is particularly concerning as there is evidence to suggest that males are less likely to self-identify or be identified with eating disorders unless the illness severity is are extremely high. Additionally, eating disorder treatment centres are less likely to accept male patients (19, 20). Gender and cultural differences in help-seeking behaviours in male eating disorder patient may result in services being less accessible, contributing to worse outcomes. This highlights the need for enhanced case-identification, research and services for male eating disorder patients to improve outcomes (21). We also found that mortality risk was higher amongst younger individuals within the cohort and individuals living in the lowest income neighbourhoods, highlighting issues related to equity of access and quality of care; this warrants further investigation.

While there have been two meta-analyses estimating ED-related mortality, (5, 8) the existing literature has methodological issues including a lack of population-based surveillance data (limited to sub-regional studies and registries from restricted clinical practices(3, 22)), selection of study population, identification of cases, and small sample size.(9, 10, 17, 23-25)

Finally, our results demonstrate the degree to which patients with EDs also experience important medical conditions and co-morbidities, such as congestive heart failure, diabetes, COPD and

hypertension amongst others. Mechanisms through which EDs may have a causal impact on diverse chronic diseases have been described elsewhere. (4)

STRENGTHS AND LIMITATIONS

A major strength of our study was the use of a population-based sample, which is more representative and generalizable than cohorts based on a sample of hospitalised patients from individual treatment centres or insurance programs. An additional methodological strength was the use of the recommended SMR method, which is replicable and well established, to report excess mortality relative to the underlying population as well as controlling for sex and age through standardization (as opposed to merely reporting case-fatality rates within the clinical cohort).

One major limitation is the lack of validation of our algorithm for case-detection, which relied on hospital contact data and not outpatient contact data. This may bias towards higher severity of cases and may also truncate the time between illness identification and mortality, which could result in an overestimation of mortality rates.(26) These are limitations of all research involving clinical cohorts based on administrative or insured services data. These inherent limitations of the best data available underscore how important it is to have disease registries for eating disorders established internationally, with high quality clinical measures, which are available only in localized clinical research cohorts (22). Moreover, the lack of data on ethnicity did not allow us to produce ethnic-specific SMRs; future research should seek to address this limitation. Finally, this study included a specific group of ED diagnoses (anorexia nervosa, bulimia nervosa, and ED NOS) for which treatment is available in Ontario's publicly funded system. We did not include other eating disorder diagnoses such

as binge-eating disorder, and it is unclear whether the findings from our study would generalize to a broader array of eating disorder diagnoses.

IMPACT AND RELEVANCE

In summary, our study provides evidence of the high mortality rate associated with eating disorder diagnoses. Furthermore, males with eating disorders have a higher risk of mortality than females, which underscores the importance of detecting and treating eating disorders in males even though they are relatively low in prevalence. These findings are consistent with previous research on excess mortality; we effectively show the marked gender differences in risk of mortality and actual excess mortality in the eating disorder population. Historically, the burden of eating disorders, including mortality, has been documented to a lesser extent compared to studies of other psychiatric conditions despite its prevalence and high mortality rate.

This study serves to highlight the need for ongoing population-based surveillance of eating disorder burden. Early intervention in eating disorders is known to be effective (27) (28) and presents an opportunity to reduce the mortality impact (high and early onset mortality) of these conditions. The inclusion of eating disorders amongst other disorders identified as high priority for improved surveillance and burden of disease data in mental health also highlights a need for better detection of and treatment of eating disorders and associated psychiatric comorbidities to improve long-term outcomes.

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No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

Author Contribution

PC, PK, SJB, CDO, TI, and KT all contributed to the formulation of the research question and study design. PK, SJB, CDO, and TI oversaw the data analysis, TI analyzed the data at ICES. SJB and TI drafted the manuscript. All authors contributed to review of the manuscript and approve of the final submission.

Data Availability

The dataset from this study is held securely in coded form at ICES. While data sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those

who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS. The full dataset creation plan and underlying analytic code are available upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

Declaration of Interest: None

REFERENCES

1. de Oliveira C, Colton P, Cheng J, Olmsted M, Kurdyak P. The direct health care costs of eating disorders among hospitalized patients: A population-based study. International Journal of Eating Disorders. 2017; 50(12): 1385-93.

2. Hudson JI, Hiripi E, Pope HG, Kessler RC. The Prevalence and Correlates of Eating Disorders in the National Comorbidity Survey Replication. Biological Psychiatry. 2007; 61(3): 348-58.

3. Fichter MM, Quadflieg N. Mortality in eating disorders - results of a large prospective clinical longitudinal study. International Journal of Eating Disorders. 2016; 49(4): 391-401.

4. E Mitchell J, Scott Crow. Medical complications of anorexia nervosa and bulimia nervosa. Current Opinion in Psychiatry. 2006; 19(4): 438-43.

5. Arcelus; J, Mitchell; AJ, Wales; J, Nielsen S. Mortality Rates in Patients With Anorexia Nervosa and Other Eating Disorders: A Meta-analysis of 36 Studies. Archives of General Psychiatry. 2011; 68(7): 724-31.

6. Udo T, Grilo CM. Prevalence and Correlates of DSM-5–Defined Eating Disorders in a Nationally Representative Sample of U.S. Adults. Biological Psychiatry. 2018; 84(5): 345-54.

7. Smink FRE, van Hoeken D, Donker GA, Susser ES, Oldehinkel AJ, Hoek HW. Three decades of eating disorders in Dutch primary care: decreasing incidence of bulimia nervosa but not of anorexia nervosa. Psychological Medicine. 2015; 46(6): 1189-96.

8. Keshaviah A, Edkins K, Hastings ER, Krishna M, Franko DL, Herzog DB, et al. Re-examining premature mortality in anorexia nervosa: a meta-analysis redux. Compr Psychiatry. 2014; 55(8): 1773-84.

9. Smink FRE, van Hoeken D, Hoek HW. Epidemiology of Eating Disorders: Incidence, Prevalence and Mortality Rates. Current Psychiatry Reports. 2012; 14(4): 406-14.

10. Keel PK, Dorer DJ, Eddy KT, Franko D, Charatan DL, Herzog DB. Predictors of Mortality in Eating Disorders. JAMA Psychiatry. 2003; 60(2): 179-83.

11. Simon J, Schmidt U, Pilling S. The health service use and cost of eating disorders. Psychological Medicine. 2005; 35(11): 1543-51.

12. Striegel-Moore RH. Health services research in anorexia nervosa. International Journal of Eating Disorders. 2005; 37 Suppl: S31-4; discussion S41-2.

13. C. Davies SJ, Tomisin Iwajomo, Oliveira Claire D, Judith Versloot, J. Reid R, Paul Kurdyak. The impact of psychiatric and medical comorbidity on the risk of mortality: a population-based analysis. Psychological Medicine. 2019: 1-9.

14. Kurdyak P, de Oliveira C, Iwajomo T, Bondy S, Trottier K, Colton P. Identifying Individuals with Eating Disorders Using Health Administrative Data. Canadian journal of psychiatry Revue canadienne de psychiatrie. 2019: 706743719844183.

15. Breslow N, Day N. Statistical Methods in Cancer Research. Volume II. The Design and Analysis of Cohort Studies. International Agency for Research on Cancer, 1987.

16. Canada S. Health Indicators 2008. Statistics Canada, 2008.

17. Kask J, Ramklint M, Kolia N, Panagiotakos D, Ekbom A, Ekselius L, et al. Anorexia nervosa in males: excess mortality and psychiatric co-morbidity in 609 Swedish in-patients. Psychological Medicine. 2017; 47(8): 1489-99.

18. Møller-Madsen S, Nystrup J, Nielsen S. Mortality in anorexia nervosa in Denmark during the period 1970-1987. Acta Psychiatrica Scandinavica. 1996; 94(6): 454-9.

19. Mond J, Mitchison D, Hay P. Eating disordered behavior in men: Prevalence, impairment in quality of life, and implications for prevention and health promotion. In: Current findings on males with eating disorders: 195-215. Routledge/Taylor & Francis Group, 2014.

20. Murray SB, Nagata JM, Griffiths S, Calzo JP, Brown TA, Mitchison D, et al. The enigma of male eating disorders: A critical review and synthesis. Clinical Psychology Review. 2017; 57(Complete): 1-11.

21. Strother E, Lemberg R, Stanford SC, Turberville D. Eating Disorders in Men: Underdiagnosed, Undertreated, and Misunderstood. Eating Disorders. 2012; 20(5): 346-55.

22. Pinhas L, Morris A, Crosby RD, Katzman DK. Incidence and age-specific presentation of restrictive eating disorders in children: a Canadian Paediatric Surveillance Program study. Archives of Pediatrics & Adolescent Medicine. 2011; 165(10): 895-9.

23. Hart LM, Mitchison D, Hay PJ. The case for a national survey of eating disorders in Australia. Journal of eating disorders. 2018; 6: 30.

24. Austin SB, Hutcheson R, Wickramatilake-Templeman S, Velasquez K. The Second Wave of Public Policy Advocacy for Eating Disorders: Charting the Course to Maximize Population Impact. The Psychiatric clinics of North America. 2019; 42(2): 319-36.

25. Keski-Rahkonen A, Mustelin L. Epidemiology of eating disorders in Europe: prevalence, incidence, comorbidity, course, consequences, and risk factors. Curr Opin Psychiatry. 2016; 29(6): 340-5.

26. Swanson SA, Field AE. Commentary: Considerations for the use of registry data to study adolescent eating disorders. International Journal of Epidemiology. 2016; 45(2): 488-90.

27. Arcelus J, Bouman WP, Morgan JF. Treating young people with eating disorders: transition from child mental health to specialist adult eating disorder services. European Eating Disorders Review: The Professional Journal of the Eating Disorders Association. 2008; 16(1): 30-6.

28. Currin L, Schmidt U. A critical analysis of the utility of an early intervention approach in the eating disorders. Journal of Mental Health. 2005; 14(6): 611-24.

405 Tables and Figures

406 Table 1: Demographic and Clinical Characteristics of the Eating Disorder cohort

VARIABLE	Female	Male	TOTAL	P-VALUE Sex differences (unadjusted)
	N=17,108	N=1,933	N=19,041	
Age at first diagnosis, ***Mean ± SD***	*25.76 ± 15.44*	*37.37 ± 23.91*	*26.94 ± 16.87*	<0.001
	N (% of cohort, females)	N (% of cohort, males)	N (% of cohort)	
Age group at diagnosis				
10_13	1,359 (7.9)	197 (10.2)	1,556 (8.2)	
14_17	5,613 (32.8)	370 (19.1)	5,983 (31.4)	
18_24	4,015 (23.5)	279 (14.4)	4,294 (22.6)	
25_44	4,231 (24.7)	443 (22.9)	4,674 (24.5)	
45_64	1,201 (7.0)	279 (14.4)	1,480 (7.8)	
65_84	519 (3.0)	290 (15.0)	809 (4.2)	
>=85	170 (1.0)	75 (3.9)	245 (1.3)	
Neighbourhood Income Quintile				
1 (low)	3,164 (18.5)	434 (22.5)	3,598 (18.9)	<0.001
2 (medium-low)	3,149 (18.4)	366 (18.9)	3,515 (18.5)	
3 (medium)	3,143 (18.4)	365 (18.9)	3,508 (18.4)	
4 (medium-high)	3,460 (20.2)	377 (19.5)	3,837 (20.2)	
5 (high)	4,105 (24.0)	374 (19.3)	4,479 (23.5)	
Missing	87 (0.5)	17 (0.9)	104 (0.5)	
Rural residence				
No	15,186 (88.8)	1,710 (88.5)	16,896 (88.7)	0.691
Yes	1,922 (11.2)	223 (11.5)	2,145 (11.3)	
Clinical Characteristics				
Eating Disorder Diagnosis at cohort entry				
AN and BN	121 (0.7)	7 (0.4)	128 (0.7)	<0.001
AN and EDNOS	*	*	55 (*)	
AN only	5,437 (31.8)	398 (20.6)	5,835 (30.6)	
AN, BN, and EDNOS	291 (1.7)	7 (0.4)	298 (1.6)	
BN and EDNOS	2,981 (17.4)	353 (18.3)	3,334 (17.5)	
BN only	2,218 (13.0)	137 (7.1)	2,355 (12.4)	
EDNOS only	6,008 (35.1)	1,028 (53.2)	7,036 (37.0)	
Co-morbidity				
Asthma	4,759 (27.8)	480 (24.8)	5,239 (27.5)	0.005
Cancer	638 (3.7)	225 (11.6)	863 (4.5)	<0.001
COPD	1,237 (7.2)	300 (15.5)	1,537 (8.1)	<0.001

Congestive Heart Failure	472 (2.8)	190 (9.8)	662 (3.5)	<0.001
Diabetes	1,390 (8.1)	343 (17.7)	1,733 (9.1)	<0.001
HIV	23 (0.1)	22 (1.1)	45 (0.2)	<0.001

Legend: SD-standard deviation; AN-Anorexia Nervosa; BN-Bulimia Nervosa; EDNOS-Eating Disorder Not Otherwise Specified; COPD- Chronic Obstructive Pulmonary Disease; HIV, Human Immuno-Deficiency Virus

411 Table 2 All-cause mortality comparing the ED cohort to the Ontario population overall and by sex. *

Age group	Person Years (in 1000's)	Observed deaths	Expected deaths	Crude mortality rates (per1,000)	SMR* (per 1000)(95% CI)
Both Sexes					
Overall	155,921.03	1672	330.85	10.88	5.1 (4.8-5.3)
15-19	22,842.62	32	6.72	1.42	4.8 (3.3-6.7)
20-24	29,121.61	59	11.57	2.04	5.1 (4.0-6.6)
25-29	25,621.18	68	10.22	2.66	6.7 (5.3-8.4)
30-34	20,068.30	84	12.04	4.19	7.0 (5.6-8.6)
35-39	14,937.13	92	10.46	6.16	8.8 (7.2-10.8)
40-44	11,810.93	107	12.99	9.06	8.2 (6.8-10.0)
45-49	9,362.66	126	16.85	13.46	7.5 (6.3-8.9)
50-54	6,407.25	116	19.86	18.10	5.8 (4.9-7.0)
55-59	3,871.77	90	18.58	23.25	4.8 (3.9-6.0)
60-64	2,232.77	83	16.3	37.17	5.1 (4.1-6.3)
65-69	1,331.44	105	15.44	78.86	6.8 (5.6-8.2)
70-74	1,012.38	113	18.53	111.62	6.1 (5.1-7.3)
75-79	875.12	137	26.78	156.55	5.1 (4.3-6.1)
80-84	765.24	180	40.25	235.22	4.5 (3.9-5.2)
85-89	474.79	172	42.87	362.26	4.0 (3.5-4.7)
90+	292.76	104	51.06	355.24	2.0 (1.7-2.5)
Female					
Overall	142,655.30	1249	272.29	8.83	4.6 (4.3-4.9)
15-19	20980.86	25	6.21	1.20	4.0 (2.7-6.0)
20-24	27195.17	50	10.83	1.85	4.6 (3.5-6.1)
25-29	24203.29	61	9.66	2.53	6.3 (4.9-8.1)
30-34	18855.12	71	11.31	3.77	6.3 (5.0-7.9)
35-39	13822.51	80	9.68	5.79	8.3 (6.6-10.3)
40-44	10747.7	90	11.82	8.37	7.6 (6.2 -9.4)
45-49	8479.574	106	15.26	12.50	7.0 (5.7-8.4)
50-54	5761.355	94	17.86	16.32	5.3 (4.3-6.4)
55-59	3433.343	73	16.48	21.26	4.4 (3.5-5.6)
60-64	1861.803	61	13.59	32.76	4.5 (3.5-5.8)
65-69	1048.189	70	12.16	66.78	5.8 (4.6-7.3)
70-74	755.4538	67	13.82	88.69	4.9 (3.8-6.2)
75-79	653.2047	85	19.99	130.13	4.3 (3.4-5.3)
80-84	583.2382	114	30.68	195.46	3.7 (3.1-4.5)
85-89	348.6016	119	31.48	341.36	3.8 (3.2-4.5)
90+	236.0726	80	41.17	338.88	1.9 (1.6-2.4)
Male					

Overall	1,213.18	423	58.56	34.56	7.2 (6.6-8.0)
15-19	1861.75	7	0.5	4.17	13.9 (6.6-29.2)
20-24	1926.44	9	0.74	4.85	12.1 (6.3-23.3)
25-29	1417.89	7	0.56	5.00	12.5 (6.0-26.2)
30-34	1213.182	13	0.73	10.72	17.9 (10.4-30.8)
35-39	1114.625	12	0.78	10.77	15.4 (8.7-27.1)
40-44	1063.231	17	1.17	15.99	14.5 (9.0-23.4)
45-49	883.0904	20	1.59	22.65	12.6 (8.1-19.5)
50-54	645.8871	22	2	34.06	11.0 (7.2-16.7)
55-59	438.4278	17	2.1	38.77	8.1 (5.0-13.0)
60-64	370.974	22	2.71	59.30	8.1 (5.4-12.3)
65-69	283.245	35	3.29	123.57	10.7 (7.7-14.8)
70-74	256.9281	46	4.7	179.04	9.8 (7.3-13.1)
75-79	221.9124	52	6.79	234.33	7.7 (5.8-10.1)
80-84	182.0007	66	9.57	362.64	6.9 (5.4-8.8)
85-89	126.1937	53	11.4	419.99	4.7 (3.6-6.1)
90+	56.68994	24	9.89	423.36	2.4 (1.6-3.6)

*SMRs are stratified by age-group where age is a time-dependent covariate reflecting age attained during follow-up as opposed to at baseline. Time-dependent age calculated using STATA command STSPLIT.

Legend: SMR - standardized mortality ratio; CI – confidence interval

Table 3 Predictors of relative excess mortality from Cox survival models for all-cause mortality within eating disordered cohort.

	Unadjusted Hazard Ratio	95% Confidence Interval	Adjusted Hazard Ratio	Hazard Ratio 95% Confidence Interval	P-value* (degrees of freedom)
Age** 10 to 44- N=16,507					
Age** (integer, continuous)	1.07	(1.06 – 1.07)	1.05	(1.05 – 1.06)	< 0.001 (1)
Calendar year (integer, continuous)	0.90	(0.89 – 0.90)	0.91	(0.91 – 0.92)	< 0.001 (1)
Sex (male versus female)	2.06	(1.92 – 2.21)	1.91	(1.78 – 2.05)	< 0.001 (1)
Neighbourhood income quintile					
1 (low)	1.36	(1.27 – 1.46)	1.26	(1.18 – 1.35)	< 0.001 (4)
2 (medium-low)	0.83	(0.76 – 0.89)	0.81	(0.75 – 0.87)	< 0.001 (4)
3 (medium)	0.95	(0.88 – 1.01)	0.97	(0.89 –1.04)	0.39 (4)
4 (medium-high)	0.96	(0.89 – 1.03)	0.98	(0.91 –1.05)	0.54 (4)
5 (high)			1.00	Reference-	
Rural residence (versus urban residence)	0.65	(0.60 – 0.71)	0.69	(0.63 - 0.75)	< 0.001 (1)
Medical co-morbidity indicators (binary):					
Congestive heart failure			2.45	(2.23 – 2.69)	< 0.001 (1)
COPD			1.07	(0.99 – 1.14)	0.07 (1)
Cancer			2.43	(2.25 – 2.62)	< 0.001 (1)
Asthma			1.01	(0.96 – 1.06)	0.76 (1)
Diabetes			1.75	(1.65 – 1.86)	< 0.001 (1)
HIV			2.16	(1.75 – 2.67)	< 0.001 (1)
Age** 45 and older- N=2532					
Age** (integer, continuous)	1.08	(1.08 – 1.08)	1.07	(1.07 – 1.08)	< 0.001 (1)
Calendar year (integer, continuous)	0.88	(0.87 – 0.88)	0.89	(0.88 – 0.89)	< 0.001 (1)
Sex (male versus female)	1.92	(1.82 – 2.01)	1.91	(1.82 – 2.02)	< 0.001 (1)
Neighbourhood income quintile:					
1 (low)	1.47	(1.37 – 1.56)	1.33	(1.25 – 1.42)	< 0.001 (4)
2 (medium-low)	1.11	(1.04 – 1.19)	1.01	(0.94 – 1.08)	0.86 (4)
3 (medium)	1.04	(0.97 – 1.11)	0.93	(0.86 – 0.99)	0.04 (4)
4 (medium-high)	0.85	(0.79 – 0.91)	0.79	(0.74 – 0.85)	< 0.001 (4)
5 (high)			1.00	Reference-	
Rural residence (versus urban residence)	1.27	(1.19 – 1.35)	1.22	(1.15 – 1.30)	< 0.001 (1)
Medical co-morbidity indicators (binary):					
Congestive heart failure			1.32	(1.25 – 1.38)	< 0.001 (1)
COPD			1.06	(1.01 – 1.11)	< 0.03 (1)
Cancer			2.24	(2.14 – 2.35)	< 0.001 (1)
Asthma			0.94	(0.89 – 0.99)	0.03 (1)
Diabetes			0.89	(0.86 – 0.94)	< 0.001 (1)
HIV			2.06	(1.59 – 2.66)	< 0.001 (1)

* Likelihood ratio test for removal of covariate from fully adjusted model shown.

** Age is defined as time-dependent covariate, meaning age of cohort member attained over follow-up and not at baseline. Time-dependent age is calculated using STATA command STSPLIT.

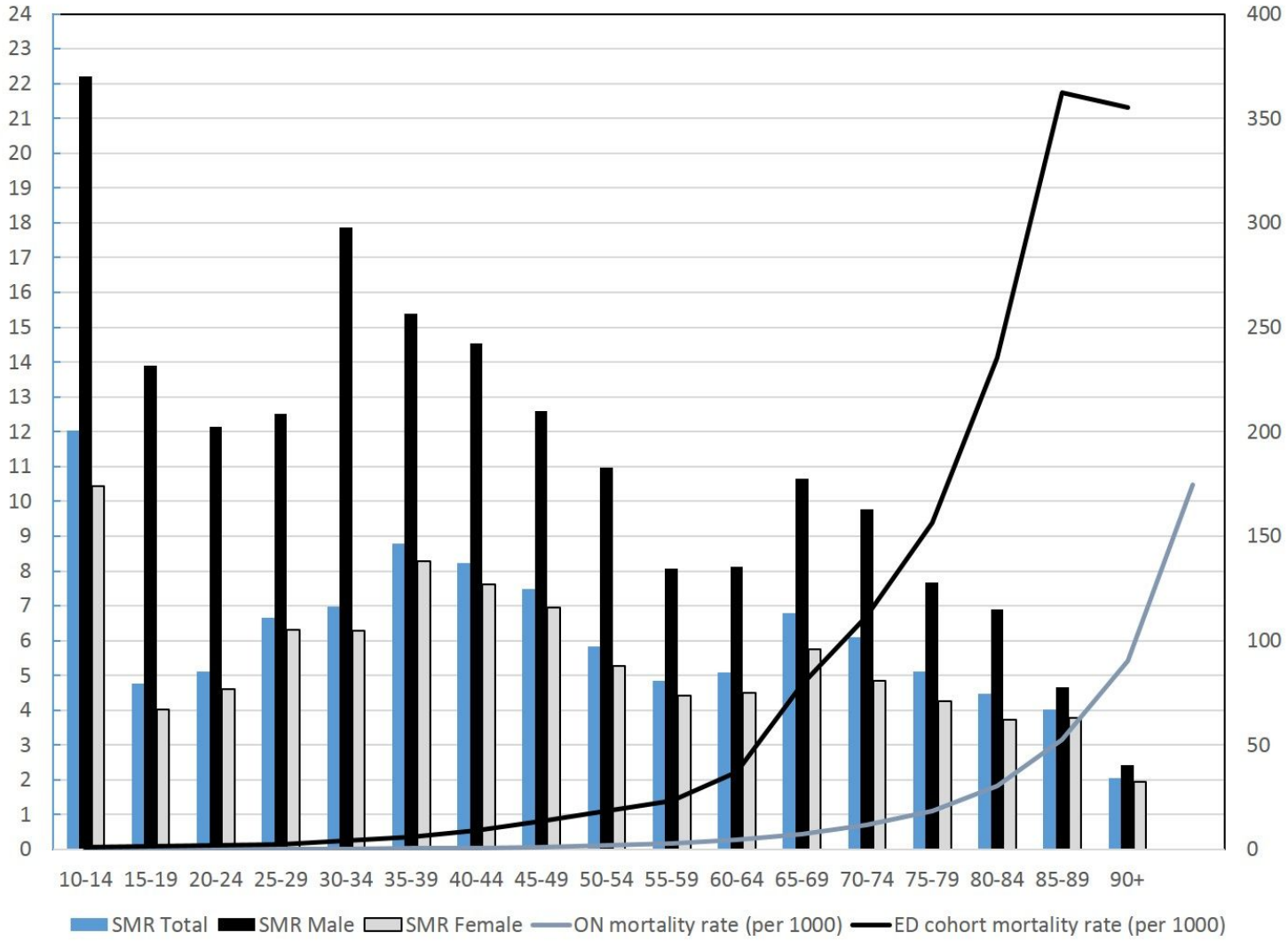
Legend: COPD- Chronic Obstructive Pulmonary Disease; HIV, Human Immuno-Deficiency Virus

Appendix Table 1: Age-Sex matched person years of life lost and 95% CI in ED cohort and Ontario population in 2011

	ED Cohort PYLL (95% CI)	Ontario Population PYLL (95% CI)	Excess PYLL (%)
Both Sexes	191.5 (189.3-193.7)	29.6 (28.8-30.5)	85%
Male	375.4 (364.4-386.6)	29.6 (28.7-30.5)	92%
Female	174.8 (172.6-177.0)	29.7 (26.6-32.7)	83%

Legend: ED – eating disorders; CI – confidence interval; PYLL – Person Years of Life Lost

Figure 1: Standardized mortality ratios-by sex and age-group, all-cause mortality rates observed within the eating disorders cohort (1991-2013) and Ontario (2011) mortality rates



Y1 axis label (left) Standardized Mortality Ratio (SMR)
Y2 axis label (right) Observed morality rate (per 1000 person years)

Excess mortality associated with eating disorders: a population-based cohort study

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Word Count : 3,519 (excludes abstract and key points)

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KEY POINTS

Question: What is the mortality rate for individuals with eating disorders?

Findings: This study of 19,041 individuals with eating disorders found that eating disorders are associated with an elevated risk of premature of death. The all-cause mortality for the entire cohort was five times higher than expected compared to the general population. Standardised mortality ratios were higher overall for males (SMR = 7.24) relative to females (SMR = 4.59).

Meaning: Individuals with eating disorders experience excess premature mortality compared to the general population. These findings highlight the need to develop focused interventions for this group to improve health outcomes.

ABSTRACT

Background

Individuals with eating disorders (EDs) have a high mortality risk. Few population-based studies have estimated mortality risk in EDs other than anorexia nervosa.

Aims

To investigate all-cause mortality within a population-based cohort of individuals who received hospital-based care for any ED (anorexia nervosa, bulimia nervosa or ED not otherwise specified) in Ontario, Canada.

Methods

We conducted a retrospective-cohort study of 19,041 individuals with an ED from January 1, 1990, to December 31, 2013 using administrative healthcare data. The outcome of interest was death. Excess mortality was assessed using standardized mortality ratios (SMRs) and potential years of life lost (PYLL). Cox proportional hazards regression models were used to examine socio-demographic and medical comorbidities associated with greater mortality risk.

Results

The ED cohort had 17,108 females (89.9%) and 1,933 males (10.1%). The all-cause mortality for the entire ED cohort was five times higher than expected compared to the Ontario population (SMR = 5.06; 95% CI:4.82-5.30). SMRs were higher for males (SMR=7.24; 95% CI: 6.58-7.96) relative to females (SMR=4.59; 95% CI: 4.34-4.85), overall, and in all age groups in the cohort. For both sexes, the ED cohort PYLL was more than 6 times higher than the expected PYLL in the Ontario population.

Conclusions and Relevance

Patients with EDs experience five to seven times higher mortality rates compared to the overall population. There is an urgent need to understand the mortality risk factors to improve health outcomes among individuals with eating disorders.

Declaration of Interest

None.

Keywords:

Eating disorders; anorexia nervosa; bulimia nervosa; EDNOS; mortality; standardized mortality ratio; male; female

WORD COUNT: 3,~~519~~ 270 (excludes abstract and key points)

Relevance Statement

Eating disorders, including anorexia nervosa, bulimia nervosa, and eating disorders not otherwise specified, are associated with high illness burden, including mortality. This study uses population-based data to estimate standardized mortality ratios (SMRs) comparing the rate of mortality amongst individuals with eating disorders to the general population in Ontario, Canada. The SMR for individuals with eating disorders was 5.06, reflecting a 5-fold increase in mortality risk for individuals with eating disorders. For males, the risk was 7-fold higher (SMR - 7.24). Understanding the risk factors for the increased mortality in eating disorders is critical to reduce mortality in this clinical population.

INTRODUCTION

Eating disorders are associated with a high risk of mortality and high illness burden including major depression, post-traumatic stress disorder, and chronic conditions including cardiovascular, heart failure, musculoskeletal and renal complications as observed in clinical population samples. (1-4) One meta-analysis reported an overall elevated mortality rate for ~~all~~ eating disorders (anorexia nervosa, bulimia nervosa, and eating disorder not otherwise specified)~~types~~, which in some instances wasere much higher than other psychiatric disorders. (5) Eating disorders have also been associated with high health care costs, related to both psychiatric and non-psychiatric hospitalizations. Previous research has found that direct health care costs for individuals hospitalised for an eating disorder were about $48 million, with higher costs for those under the age of 20 and those 65 and older. (1) However, few population-based surveillance studies estimating incidence, prevalence and mortality in eating disorders have been published (2, 6, 7), with the literature on the epidemiology and outcomes of eating disorders having significant limitations such as small sample sizes and few large-scale mental health surveillance studies.(2, 6)

Most of the literature reporting on mortality in eating disorder patients comes from studies examining cohorts in specific treatment settings, which are difficult to compare given the wide variability in treatment target populations, insurance coverage and other selection biases. (8, 9) Several mortality studies report only crude case fatality rates (i.e., they report on deaths among patients with no comparison group or adjustment for expected mortality in the same age population); other studies are limited in sample size or scope and report only on anorexia nervosa and/or only examine female patients.(9, 10) Eating disorders have been misperceived as rare perhaps due to limited awareness of the available data on the burden of disease or a misconception that only the most

severe cases experience a severe burden. (11, 12) Furthermore, the lack of comprehensive data on eating disorders that includes both males and females has made it difficult to estimate all-cause and cause-specific mortality among this population.

This study describes all-cause mortality rates within a population-based cohort of patients with an eating disorder in a context of universal public health care funding. Excess mortality among these patients wais estimated relative to the general population without an eating disorder using standardized mortality ratios (SMRs) and potential years of life lost (PYLL) (in total and attributable to eating disorders). In addition, factors associated with increased hazard of mortality within the ED cohort were examined including patient socio-demographic and comorbidity measures as well as indicators of health care service utilization.

METHODS

Study design

This study examines a population-based, retrospective cohort of individuals who received care for an eating disorder in any hospital in Ontario from January 1, 1990, to December 31, 2013. The cohort was followed, through record-linkage, until date of death or December 31, 2013, the latest date possible based on data availability at the time of the analysis).

Data sources

We made use of administrative health care data available through ICES in Toronto, Ontario. ICES is an independent non-profit organization funded by the Ontario Ministry of Health and holds an inventory of coded and linkable health datasets, encompassing much of the publicly funded administrative health services records for the Ontario population eligible for universal health coverage

since 1986. This data repository includes individual-level, linkable longitudinal data on most publicly funded health care services. The Registered Persons Database (RPDB), a population-based registry, contains anonymized demographic data on all insured members of the universal Ontario Health Insurance Plan (OHIP), such as sex, date of birth, urban or rural dwelling information and neighbourhood-level income (measured in quintiles at the census tract level). Information on date and cause of death (where applicable) were obtained from the Ontario Registry General-Death Vital Statistics. Hospital admissions and associated diagnostic codes used to define the cohort were obtained from the following health care administrative databases maintained by the Canadian Institute for Health Information: Discharge Abstract Database (DAD) for non-mental health admissions and National Ambulatory Care Reporting System (NACRS) for emergency department visits. Psychiatric hospitalization records were obtained from the Ontario Mental Health Reporting System (OMHRS) database.

Co-morbidity data for chronic medical conditions were obtained via the following validated patient cohorts and registries developed, linked and analyzed at ICES including: Ontario Congestive Heart Failure (CHF) Database; Chronic Obstructive Pulmonary Disease (COPD) Database; Ontario Diabetes Database (ODD); Ontario Asthma Database; Ontario HIV Database and Ontario Cancer Registry (OCR). These datasets have been described elsewhere. (13)

Derivation of the eating disorder patient cohort

Individuals were included if they received an eating disorder diagnosis during an emergency department visit, medical hospitalization, or psychiatric hospitalization from 1990 to 2013. The first diagnosis from any of these data sources was determined as the cohort entry date. Cohort development and analyses were carried out with linked administrative health care data holdings at

ICES. Diagnostic codes used to identify eating disorder patients included: ICD-9 codes 307.1 (anorexia nervosa), 307.51 (bulimia nervosa), 307.50 (eating disorders not otherwise specified); ICD-10 codes F50.0 (eating disorders), F50.1 (anorexia nervosa), F50.2, F50.3 (bulimia nervosa), F50.8, F50.9 (EDNOS), and DSM-IV codes 307.1 (anorexia nervosa), 307.51 (bulimia nervosa), 307.50 (EDNOS). We restricted our study to these three ED diagnoses because the publicly-funded services in Ontario focus on the treatment of these ED diagnoses. ED diagnosis codes do not apply to children under the age of 5. Furthermore, children ages 5 to 9 were excluded as the small number of deaths precluded reporting under Ontario privacy regulations. We excluded individuals who ceased to be publicly insured for health care at date of cohort entry. This approach resulted in a cohort of 19,041 individuals with and eating disorder diagnosis (including all patients deceased or alive to the end of December 31, 2013).

The development of this cohort, restricted to individuals alive as of January 1,2014, has also been described elsewhere. (14)

Analysis

Mortality rates were estimated for the full cohort and were reported as deaths per 1,000 person-years of observation time, overall and by sex (female and male), calendar year (from 1990 to 2013), and age groups. Person-years of follow-up were segregated by sex, calendar year and age attained over follow-up (to end of follow-up, or death) for each cohort member. This was achieved using Lexis expansion tools for cohort data using Stata 14 (StataCorp. 2015. *Stata Statistical Software: Release 14*. College Station, TX: StataCorp LP). Excess mortality in the eating disorder population, relative to the underlying Ontario population, was illustrated in several ways including SMRs, PYLL in the cohort, and proportion of PYLL attributable to eating disorder.

SMRs were estimated using the indirect method.(15) SMRs were defined as the number of observed deaths in the eating disorder cohort divided by the number of expected deaths in the cohort if the eating disorder cohort had had the same sex- and age-specific mortality experience as the underlying Ontario population. Expected mortality rates in the general population were obtained using all Ontario deaths in 2011 and corresponding data for the 2011 Census year. SMRs were presented with exact Poisson-based 95% confidence intervals.

Person Years of Life Lost (PYLL) within the eating disorder cohort were estimated as the sum of all years of life lost before age 75 (16) for observed deaths among patients with an eating disorder (expressed as PYLL per 1,000 persons). Expected and excess (eating disorder attributable) PYLL values were also estimated using expected deaths from Ontario 2011 standard mortality rates. The theoretical percent of total PYLL attributable to being in the eating disorder cohort (relative to the underlying population) was defined as attributable PYLL = (total cohort PYLL – expected PYLL)/ total cohort PYLL and expressed as a percentage.

Socio-demographic factors associated with higher risk of mortality within the cohort were examined using Cox Proportional Hazard regression models for all-cause mortality. Patients who entered the cohort with an eating disorder diagnosis on the same day as death contributed no follow-up time and were excluded from the survival models (N=5). Separate Cox models were estimated for patients aged 10 to 44 at entry and those 45 and older. Patient socio-demographic characteristics considered were age, sex and calendar year over the period of the study, as well as neighbourhood-level household income quintile and rurality of residence. Models examining the effect of socio-demographic variables were then further adjusted for medical co-morbidity (i.e., chronic conditions,

defined beforehand). The adjusted models included six chronic conditions derived from validated cohorts through administrative databases.

Model diagnostics were performed and indicated no violations of assumptions. This included confirmation of the validity of a linear effect of age as a continuous covariate in the exponential Cox model, assessment for non-violation of the assumption of proportional hazards, and lack of excess multi-collinearity.

Ethics and approvals

ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. Thus, the use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. The project was approved by the Research Ethics Board at University Health Network, Toronto.

RESULTS

Baseline characteristics of the eating disorder cohort are presented in Table 1. Of the 19,041 cohort members, 17,108 were female (89.9%) and 1,933 were male (10.1%). Age at cohort entry ranged from 10 to over 85 years of age, but 88.9% of the population entered the cohort between the ages of 14 and 44. Most of the cohort (88.8%) resided in urban centres. A greater percentage of the cohort lived in middle to low-income neighbourhoods, with 37.4% in the lowest neighbourhood level income category and 18.0% in the middle-income neighbourhood level income category. Categories for eating disorder--specific diagnoses at cohort entry revealed multiple diagnoses for the same individual over time; 31.8% of the cohort had anorexia nervosa alone or in combination with bulimia nervosa and/or eating disorder not otherwise specified (EDNOS); 35.1% of the cohort had a diagnosis of EDNOS alone at enrolment. Eating disorder diagnoses were also comorbid with other medical conditions including asthma (27.0%), diabetes (8.9%), cancer (4.6%) and congestive heart failure (3.5%).

Table 2 presents descriptive statistics for the mortality follow-up analysis of this cohort, including total person-years of follow up and observed deaths, for the whole cohort and by age group and sex. Mortality rates and SMRs by age group and sex are also presented in Table 2. For the entire eating disorder cohort and across all age groups, the all-cause mortality rate was five times higher than expected based on mortality rates in the Ontario population (marginal SMR = 5.06; 95% CI:4.82-5.30). Peak values for SMRs were observed among adults from approximately 30 to 44 years of age. Mortality rates and SMRs were unstable for individuals 10 to 14 due to small number of deaths. SMRs were higher for male eating disorder patients, relative to female, overall and in all age groups. For females, the marginal SMR was 4.59 (95% CI: 4.34-4.85) while for males it was 7.24 (95% CI: 6.58-7.96).

Excess mortality is further illustrated in Figure 1, which presents cohort and population mortality rates (per 1,000 population) by age and sex as well as age-sex specific SMRs.

The overall expected PYLL (based on expected numbers of deaths in the cohort using the 2011 Ontario age-specific death rates) was estimated at 29.54 years per 1,000 population (95% CI: 28.7-30.4) and similar for each sex separately (Appendix Table 1). Within the eating disorder cohort, estimated total PYLL before age 75 equalled 191.6 per 1,000 population (95% CI: 189.4-193.8), for both sexes, combined. Years of life lost per 1,000 population was higher for males (PYLL within cohort=375.6; 95% CI: 364.7-386.8) relative to females (PYLL within cohort=174.1; 95% CI: 171.9-176.3). For both sexes, the excess PYLL attributable to experiencing an eating disorder was 84%. For female eating disorder patients, it was estimated that 83% of PYLL were attributable to being in the eating disorder cohort; for male eating disorder patients, this value was 92%. Among all Ontario ED patients, over the period of this study, it was estimated that 24,773 years of life were lost due to eating disorder, before the age of 75.

Cox survival models on all-cause mortality, controlling for the effects of demographic characteristics, appear in Table 3. For both age groups (10-44 and >=45 years of age), older age (as a continuous, linear term) and male sex were associated with statistically significant increased mortality risk and adjusted hazard ratio of 1.91 in both age groups. Additionally, mortality declined over calendar years in the analysis showing a statistically significant effect of calendar year on the downward trend in mortality over time (adjusted hazard ratio of 0.9, year over year). In addition, the pattern of association with household income quintile was not a simple linear association, but rather a U-shaped pattern. Higher total mortality hazard ratios were observed in the highest and lowest income quintiles, relative to household income quintiles in the middle.

Fully adjusted models for age, sex and calendar year resulted in opposite findings for rurality in the analyses for cohort members under and over 45 years of age. Rural residence was associated with lower mortality for cohort members under the age of 45 but higher mortality risk for cohort members 45 or older. Control variables for non-ED chronic medical conditions (CHF, COPD, cancer and HIV) were all positively associated with higher mortality ratios with the exceptions of inverse associations for asthma and diabetes diagnoses within cohort members age 45 and over. For cohort members ages 44 and younger, having a diagnosis of CHF, cancer, diabetes and HIV was positively associated with higher mortality ratios. We observed a simple linear trend toward lower mortality with calendar year of entry into the cohort. This cannot be separated from a general trend in improved survival in the population as age-sex specific mortality risk expected in the population are not updated for each calendar year but based on census years (here based on the 2011 Canadian census).

DISCUSSION

The purpose of this study was to estimate the excess mortality and burden associated with eating disorders using comprehensive population-based data. Notably, this study is among the few internationally that have made use of a population-based eating disorder cohort and to have provided SMR estimates specific to both female and male patients. Our findings show that individuals with eating disorders diagnosed in hospital settings had a mortality rate of approximately 5-fold higher than the general population, with more than 80% of life lost before the age of 75 for females and males.

In female eating disorder patients, we found a roughly five-fold mortality rate relative to the general population. This is similar in magnitude to what has been reported in two international meta-analyses (5, 8) and similar in magnitude to SMRs reported specifically for anorexia nervosa (anorexia

nervosa being the eating disorder diagnosis with the highest SMRs). Whilst studies have reported on the lifetime prevalence of eating disorders in males ranging from 0.1 to 2.0 for all types,(2, 9) few studies have reported on the mortality rates among males with eating disorders and those studies tend to report exclusively on anorexia nervosa.(17, 18) Our study thus makes a novel and important contribution to the sparse literature on male eating disorder patients and their mortality experience, with a substantially larger sample of male eating disorder patients.

The SMRs observed in males were almost 2-fold higher than in females. This observation of higher mortality in males with eating disorders is particularly concerning as there is evidence to suggest that males are less likely to self-identify or be identified with eating disorders unless the illness severity isse are extremely high severe.; Aadditionally, , eating disorder treatment centres are less likely to accept or treat male patients (19, 20). Poorer outcomes in male patients with eating disorders may reflect gGender and cultural differences in help-seeking behaviours or referral patterns indicating thatin male eating disorder patient may result in services for male patients arebeing less accessible, and thus ccontributinge to worse outcomes. This highlights the need for enhanced case-identification, research and services for male eating disorder patients to improve outcomes (21). We also found that mortality risk was higher amongst younger individuals within the cohort and individuals living in the lowest income neighbourhoods, highlighting issues around potential accessrelated to equity of access and quality of care; this warrants further investigation.

While there have been two meta-analyses estimating ED-related mortality, (5, 8) the existing literature has methodological issues including a lack of population-based surveillance data (limited to sub-regional studies and registries from restricted clinical practices(3, 22)), selection of study population, identification of cases, and small sample size.(9, 10, 17, 23-25)

Finally, our results demonstrate the degree to which patients with EDs also experience important medical conditions and co-morbidities, such as congestive heart failure, diabetes, COPD and hypertension amongst others. Mechanisms through which EDs may have a causal impact on diverse chronic diseases have been described elsewhere. (4)

STRENGTHS AND LIMITATIONS

A major strength of our study was the use of a population-based sample, which is more representative and generalizable than cohorts based on a sample of hospitalised patients from individual treatment centres or insurance programs. An additional methodological strength was the use of the recommended SMR method, which is replicable and well established, to report excess mortality relative to the underlying population as well as controlling for sex and age through standardization (as opposed to merely reporting case-fatality rates within the clinical cohort).

One major limitation is the lack of validation of our algorithm for case-detection, which relied on hospital contact data and not outpatient contact data. This may bias towards higher severity of cases and may also truncate the time between illness identification and mortality, which could result in an overestimation of mortality rates.(26) These are limitations of all research involving clinical cohorts based on administrative or insured services data. These inherent limitations of the best data available underscore how important it is to have disease registries for eating disorders established internationally, with high quality clinical measures, which are available only in localized clinical research cohorts (22). Moreover, the lack of data on ethnicity did not allow us to produce ethnic-specific SMRs; future research should seek to address this limitation. Finally, this study included a specific group of ED diagnoses (anorexia nervosa, bulimia nervosa, and ED NOS) for which treatment is

available in Ontario's publicly funded system. We did not include other eating disorder diagnoses such as binge-eating disorder, and it is unclear whether the findings from our study would generalize to a broader array of eating disorder diagnoses.

IMPACT AND RELEVANCE

In summary, our study provides evidence of the high mortality rate associated with eating disorder diagnoses. Furthermore, males with eating disorders have a higher risk of mortality than females, which underscores the importance of detecting and treating eating disorders in males even though they are relatively low in prevalence. These findings are consistent with previous research on excess mortality; we effectively show the marked gender differences in risk of mortality and actual excess mortality in the eating disorder population. Historically, the burden ~~including mortality,~~ of eating disorders, including mortality, has been documented to a lesser extent compared to studies of other psychiatric conditions despite its prevalence and high mortality rate.

This study serves to highlight the need for ongoing population-based surveillance of eating disorder burden. Early intervention in eating disorders is known to be effective (27) (28) and presents an opportunity to reduce the mortality impact (high and early onset mortality) of these conditions. The inclusion of eating disorders amongst other disorders identified as high priority for improved surveillance and burden of disease data in mental health also highlights a need for better detection of and treatment of eating disorders and associated psychiatric comorbidities to improve long-term outcomes.

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No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

Author Contribution

PC, PK, SJB, CDO, TI, and KT all contributed to the formulation of the research question and study design. PK, SJB, CDO, and TI oversaw the data analysis, TI analyzed the data at ICES. SJB and TI drafted the manuscript. All authors contributed to review of the manuscript and approve of the final submission.

Data Availability

The dataset from this study is held securely in coded form at ICES. While data sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those

who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS. The full dataset creation plan and underlying analytic code are available upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

Declaration of Interest: None

REFERENCES

1. de Oliveira C, Colton P, Cheng J, Olmsted M, Kurdyak P. The direct health care costs of eating disorders among hospitalized patients: A population-based study. International Journal of Eating Disorders. 2017; 50(12): 1385-93.

2. Hudson JI, Hiripi E, Pope HG, Kessler RC. The Prevalence and Correlates of Eating Disorders in the National Comorbidity Survey Replication. Biological Psychiatry. 2007; 61(3): 348-58.

3. Fichter MM, Quadflieg N. Mortality in eating disorders - results of a large prospective clinical longitudinal study. International Journal of Eating Disorders. 2016; 49(4): 391-401.

4. E Mitchell J, Scott Crow. Medical complications of anorexia nervosa and bulimia nervosa. Current Opinion in Psychiatry. 2006; 19(4): 438-43.

5. Arcelus; J, Mitchell; AJ, Wales; J, Nielsen S. Mortality Rates in Patients With Anorexia Nervosa and Other Eating Disorders: A Meta-analysis of 36 Studies. Archives of General Psychiatry. 2011; 68(7): 724-31.

6. Udo T, Grilo CM. Prevalence and Correlates of DSM-5–Defined Eating Disorders in a Nationally Representative Sample of U.S. Adults. Biological Psychiatry. 2018; 84(5): 345-54.

7. Smink FRE, van Hoeken D, Donker GA, Susser ES, Oldehinkel AJ, Hoek HW. Three decades of eating disorders in Dutch primary care: decreasing incidence of bulimia nervosa but not of anorexia nervosa. Psychological Medicine. 2015; 46(6): 1189-96.

8. Keshaviah A, Edkins K, Hastings ER, Krishna M, Franko DL, Herzog DB, et al. Re-examining premature mortality in anorexia nervosa: a meta-analysis redux. Compr Psychiatry. 2014; 55(8): 1773-84.

9. Smink FRE, van Hoeken D, Hoek HW. Epidemiology of Eating Disorders: Incidence, Prevalence and Mortality Rates. Current Psychiatry Reports. 2012; 14(4): 406-14.

10. Keel PK, Dorer DJ, Eddy KT, Franko D, Charatan DL, Herzog DB. Predictors of Mortality in Eating Disorders. JAMA Psychiatry. 2003; 60(2): 179-83.

11. Simon J, Schmidt U, Pilling S. The health service use and cost of eating disorders. Psychological Medicine. 2005; 35(11): 1543-51.

12. Striegel-Moore RH. Health services research in anorexia nervosa. International Journal of Eating Disorders. 2005; 37 Suppl: S31-4; discussion S41-2.

13. C. Davies SJ, Tomisin Iwajomo, Oliveira Claire D, Judith Versloot, J. Reid R, Paul Kurdyak. The impact of psychiatric and medical comorbidity on the risk of mortality: a population-based analysis. Psychological Medicine. 2019: 1-9.

14. Kurdyak P, de Oliveira C, Iwajomo T, Bondy S, Trottier K, Colton P. Identifying Individuals with Eating Disorders Using Health Administrative Data. Canadian journal of psychiatry Revue canadienne de psychiatrie. 2019: 706743719844183.

15. Breslow N, Day N. Statistical Methods in Cancer Research. Volume II. The Design and Analysis of Cohort Studies. International Agency for Research on Cancer, 1987.

16. Canada S. Health Indicators 2008. Statistics Canada, 2008.

17. Kask J, Ramklint M, Kolia N, Panagiotakos D, Ekbom A, Ekselius L, et al. Anorexia nervosa in males: excess mortality and psychiatric co-morbidity in 609 Swedish in-patients. Psychological Medicine. 2017; 47(8): 1489-99.

18. Møller-Madsen S, Nystrup J, Nielsen S. Mortality in anorexia nervosa in Denmark during the period 1970-1987. Acta Psychiatrica Scandinavica. 1996; 94(6): 454-9.

19. Mond J, Mitchison D, Hay P. Eating disordered behavior in men: Prevalence, impairment in quality of life, and implications for prevention and health promotion. In: Current findings on males with eating disorders: 195-215. Routledge/Taylor & Francis Group, 2014.

20. Murray SB, Nagata JM, Griffiths S, Calzo JP, Brown TA, Mitchison D, et al. The enigma of male eating disorders: A critical review and synthesis. Clinical Psychology Review. 2017; 57(Complete): 1-11.

21. Strother E, Lemberg R, Stanford SC, Turberville D. Eating Disorders in Men: Underdiagnosed, Undertreated, and Misunderstood. Eating Disorders. 2012; 20(5): 346-55.

22. Pinhas L, Morris A, Crosby RD, Katzman DK. Incidence and age-specific presentation of restrictive eating disorders in children: a Canadian Paediatric Surveillance Program study. Archives of Pediatrics & Adolescent Medicine. 2011; 165(10): 895-9.

23. Hart LM, Mitchison D, Hay PJ. The case for a national survey of eating disorders in Australia. Journal of eating disorders. 2018; 6: 30.

24. Austin SB, Hutcheson R, Wickramatilake-Templeman S, Velasquez K. The Second Wave of Public Policy Advocacy for Eating Disorders: Charting the Course to Maximize Population Impact. The Psychiatric clinics of North America. 2019; 42(2): 319-36.

25. Keski-Rahkonen A, Mustelin L. Epidemiology of eating disorders in Europe: prevalence, incidence, comorbidity, course, consequences, and risk factors. Curr Opin Psychiatry. 2016; 29(6): 340-5.

26. Swanson SA, Field AE. Commentary: Considerations for the use of registry data to study adolescent eating disorders. International Journal of Epidemiology. 2016; 45(2): 488-90.

27. Arcelus J, Bouman WP, Morgan JF. Treating young people with eating disorders: transition from child mental health to specialist adult eating disorder services. European Eating Disorders Review: The Professional Journal of the Eating Disorders Association. 2008; 16(1): 30-6.

28. Currin L, Schmidt U. A critical analysis of the utility of an early intervention approach in the eating disorders. Journal of Mental Health. 2005; 14(6): 611-24.

Tables and Figures

Table 1: Demographic and Clinical Characteristics of the Eating Disorder cohort

VARIABLE	Female	Male	TOTAL	P-VALUE Sex differences (unadjusted)
	N=17,108	N=1,933	N=19,041	
Age at first diagnosis, ***Mean ± SD***	*25.76 ± 15.44*	*37.37 ± 23.91*	*26.94 ± 16.87*	<0.001
	N (% of cohort, females)	N (% of cohort, males)	N (% of cohort)	
Age group at diagnosis				
10_13	1,359 (7.9)	197 (10.2)	1,556 (8.2)	
14_17	5,613 (32.8)	370 (19.1)	5,983 (31.4)	
18_24	4,015 (23.5)	279 (14.4)	4,294 (22.6)	
25_44	4,231 (24.7)	443 (22.9)	4,674 (24.5)	
45_64	1,201 (7.0)	279 (14.4)	1,480 (7.8)	
65_84	519 (3.0)	290 (15.0)	809 (4.2)	
>=85	170 (1.0)	75 (3.9)	245 (1.3)	
Neighbourhood Income Quintile				
1 (low)	3,164 (18.5)	434 (22.5)	3,598 (18.9)	<0.001
2 (medium-low)	3,149 (18.4)	366 (18.9)	3,515 (18.5)	
3 (medium)	3,143 (18.4)	365 (18.9)	3,508 (18.4)	
4 (medium-high)	3,460 (20.2)	377 (19.5)	3,837 (20.2)	
5 (high)	4,105 (24.0)	374 (19.3)	4,479 (23.5)	
Missing	87 (0.5)	17 (0.9)	104 (0.5)	
Rural residence				
No	15,186 (88.8)	1,710 (88.5)	16,896 (88.7)	0.691
Yes	1,922 (11.2)	223 (11.5)	2,145 (11.3)	
Clinical Characteristics				
Eating Disorder Diagnosis at cohort entry				
AN and BN	121 (0.7)	7 (0.4)	128 (0.7)	<0.001
AN and EDNOS	*	*	55 (*)	
AN only	5,437 (31.8)	398 (20.6)	5,835 (30.6)	
AN, BN, and EDNOS	291 (1.7)	7 (0.4)	298 (1.6)	
BN and EDNOS	2,981 (17.4)	353 (18.3)	3,334 (17.5)	
BN only	2,218 (13.0)	137 (7.1)	2,355 (12.4)	
EDNOS only	6,008 (35.1)	1,028 (53.2)	7,036 (37.0)	
Co-morbidity				
Asthma	4,759 (27.8)	480 (24.8)	5,239 (27.5)	0.005
Cancer	638 (3.7)	225 (11.6)	863 (4.5)	<0.001
COPD	1,237 (7.2)	300 (15.5)	1,537 (8.1)	<0.001

Congestive Heart Failure	472 (2.8)	190 (9.8)	662 (3.5)	<0.001
Diabetes	1,390 (8.1)	343 (17.7)	1,733 (9.1)	<0.001
HIV	23 (0.1)	22 (1.1)	45 (0.2)	<0.001

Legend: SD-standard deviation; AN-Anorexia Nervosa; BN-Bulimia Nervosa; EDNOS-Eating Disorder Not Otherwise Specified; COPD- Chronic Obstructive Pulmonary Disease; HIV, Human Immuno-Deficiency Virus

Table 2 All-cause mortality comparing the ED cohort to the Ontario population overall and by sex. *

Age group	Person Years (in 1000's)	Observed deaths	Expected deaths	Crude mortality rates (per1,000)	SMR* (per 1000)(95% CI)
Both Sexes					
Overall	155,921.03	1672	330.85	10.88	5.1 (4.8-5.3)
15-19	22,842.62	32	6.72	1.42	4.8 (3.3-6.7)
20-24	29,121.61	59	11.57	2.04	5.1 (4.0-6.6)
25-29	25,621.18	68	10.22	2.66	6.7 (5.3-8.4)
30-34	20,068.30	84	12.04	4.19	7.0 (5.6-8.6)
35-39	14,937.13	92	10.46	6.16	8.8 (7.2-10.8)
40-44	11,810.93	107	12.99	9.06	8.2 (6.8-10.0)
45-49	9,362.66	126	16.85	13.46	7.5 (6.3-8.9)
50-54	6,407.25	116	19.86	18.10	5.8 (4.9-7.0)
55-59	3,871.77	90	18.58	23.25	4.8 (3.9-6.0)
60-64	2,232.77	83	16.3	37.17	5.1 (4.1-6.3)
65-69	1,331.44	105	15.44	78.86	6.8 (5.6-8.2)
70-74	1,012.38	113	18.53	111.62	6.1 (5.1-7.3)
75-79	875.12	137	26.78	156.55	5.1 (4.3-6.1)
80-84	765.24	180	40.25	235.22	4.5 (3.9-5.2)
85-89	474.79	172	42.87	362.26	4.0 (3.5-4.7)
90+	292.76	104	51.06	355.24	2.0 (1.7-2.5)
Female					
Overall	142,655.30	1249	272.29	8.83	4.6 (4.3-4.9)
15-19	20980.86	25	6.21	1.20	4.0 (2.7-6.0)
20-24	27195.17	50	10.83	1.85	4.6 (3.5-6.1)
25-29	24203.29	61	9.66	2.53	6.3 (4.9-8.1)
30-34	18855.12	71	11.31	3.77	6.3 (5.0-7.9)
35-39	13822.51	80	9.68	5.79	8.3 (6.6-10.3)
40-44	10747.7	90	11.82	8.37	7.6 (6.2 -9.4)
45-49	8479.574	106	15.26	12.50	7.0 (5.7-8.4)
50-54	5761.355	94	17.86	16.32	5.3 (4.3-6.4)
55-59	3433.343	73	16.48	21.26	4.4 (3.5-5.6)
60-64	1861.803	61	13.59	32.76	4.5 (3.5-5.8)
65-69	1048.189	70	12.16	66.78	5.8 (4.6-7.3)
70-74	755.4538	67	13.82	88.69	4.9 (3.8-6.2)
75-79	653.2047	85	19.99	130.13	4.3 (3.4-5.3)
80-84	583.2382	114	30.68	195.46	3.7 (3.1-4.5)
85-89	348.6016	119	31.48	341.36	3.8 (3.2-4.5)
90+	236.0726	80	41.17	338.88	1.9 (1.6-2.4)
Male					

Overall	1,213.18	423	58.56	34.56	7.2 (6.6-8.0)
15-19	1861.75	7	0.5	4.17	13.9 (6.6-29.2)
20-24	1926.44	9	0.74	4.85	12.1 (6.3-23.3)
25-29	1417.89	7	0.56	5.00	12.5 (6.0-26.2)
30-34	1213.182	13	0.73	10.72	17.9 (10.4-30.8)
35-39	1114.625	12	0.78	10.77	15.4 (8.7-27.1)
40-44	1063.231	17	1.17	15.99	14.5 (9.0-23.4)
45-49	883.0904	20	1.59	22.65	12.6 (8.1-19.5)
50-54	645.8871	22	2	34.06	11.0 (7.2-16.7)
55-59	438.4278	17	2.1	38.77	8.1 (5.0-13.0)
60-64	370.974	22	2.71	59.30	8.1 (5.4-12.3)
65-69	283.245	35	3.29	123.57	10.7 (7.7-14.8)
70-74	256.9281	46	4.7	179.04	9.8 (7.3-13.1)
75-79	221.9124	52	6.79	234.33	7.7 (5.8-10.1)
80-84	182.0007	66	9.57	362.64	6.9 (5.4-8.8)
85-89	126.1937	53	11.4	419.99	4.7 (3.6-6.1)
90+	56.68994	24	9.89	423.36	2.4 (1.6-3.6)

*SMRs are stratified by age-group where age is a time-dependent covariate reflecting age attained during follow-up as opposed to at baseline. Time-dependent age calculated using STATA command STSPLIT.

Legend: SMR - standardized mortality ratio; CI – confidence interval

Table 3 Predictors of relative excess mortality from Cox survival models for all-cause mortality within eating disordered cohort.

	Unadjusted Hazard Ratio	95% Confidence Interval	Adjusted Hazard Ratio	Hazard Ratio 95% Confidence Interval	P-value* (degrees of freedom)
Age** 10 to 44- N=16,507					
Age** (integer, continuous)	1.07	(1.06 – 1.07)	1.05	(1.05 – 1.06)	< 0.001 (1)
Calendar year (integer, continuous)	0.90	(0.89 – 0.90)	0.91	(0.91 – 0.92)	< 0.001 (1)
Sex (male versus female)	2.06	(1.92 – 2.21)	1.91	(1.78 – 2.05)	< 0.001 (1)
Neighbourhood income quintile					
1 (low)	1.36	(1.27 – 1.46)	1.26	(1.18 – 1.35)	< 0.001 (4)
2 (medium-low)	0.83	(0.76 – 0.89)	0.81	(0.75 – 0.87)	< 0.001 (4)
3 (medium)	0.95	(0.88 – 1.01)	0.97	(0.89 –1.04)	0.39 (4)
4 (medium-high)	0.96	(0.89 – 1.03)	0.98	(0.91 –1.05)	0.54 (4)
5 (high)			1.00	Reference-	
Rural residence (versus urban residence)	0.65	(0.60 – 0.71)	0.69	(0.63 - 0.75)	< 0.001 (1)
Medical co-morbidity indicators (binary):					
Congestive heart failure			2.45	(2.23 – 2.69)	< 0.001 (1)
COPD			1.07	(0.99 – 1.14)	0.07 (1)
Cancer			2.43	(2.25 – 2.62)	< 0.001 (1)
Asthma			1.01	(0.96 – 1.06)	0.76 (1)
Diabetes			1.75	(1.65 – 1.86)	< 0.001 (1)
HIV			2.16	(1.75 – 2.67)	< 0.001 (1)
Age** 45 and older- N=2532					
Age** (integer, continuous)	1.08	(1.08 – 1.08)	1.07	(1.07 – 1.08)	< 0.001 (1)
Calendar year (integer, continuous)	0.88	(0.87 – 0.88)	0.89	(0.88 – 0.89)	< 0.001 (1)
Sex (male versus female)	1.92	(1.82 – 2.01)	1.91	(1.82 – 2.02)	< 0.001 (1)
Neighbourhood income quintile:					
1 (low)	1.47	(1.37 – 1.56)	1.33	(1.25 – 1.42)	< 0.001 (4)
2 (medium-low)	1.11	(1.04 – 1.19)	1.01	(0.94 – 1.08)	0.86 (4)
3 (medium)	1.04	(0.97 – 1.11)	0.93	(0.86 – 0.99)	0.04 (4)
4 (medium-high)	0.85	(0.79 – 0.91)	0.79	(0.74 – 0.85)	< 0.001 (4)
5 (high)			1.00	Reference-	
Rural residence (versus urban residence)	1.27	(1.19 – 1.35)	1.22	(1.15 – 1.30)	< 0.001 (1)
Medical co-morbidity indicators (binary):					
Congestive heart failure			1.32	(1.25 – 1.38)	< 0.001 (1)
COPD			1.06	(1.01 – 1.11)	< 0.03 (1)
Cancer			2.24	(2.14 – 2.35)	< 0.001 (1)
Asthma			0.94	(0.89 – 0.99)	0.03 (1)
Diabetes			0.89	(0.86 – 0.94)	< 0.001 (1)
HIV			2.06	(1.59 – 2.66)	< 0.001 (1)

* Likelihood ratio test for removal of covariate from fully adjusted model shown.

** Age is defined as time-dependent covariate, meaning age of cohort member attained over follow-up and not at baseline. Time-dependent age is calculated using STATA command STSPLIT.

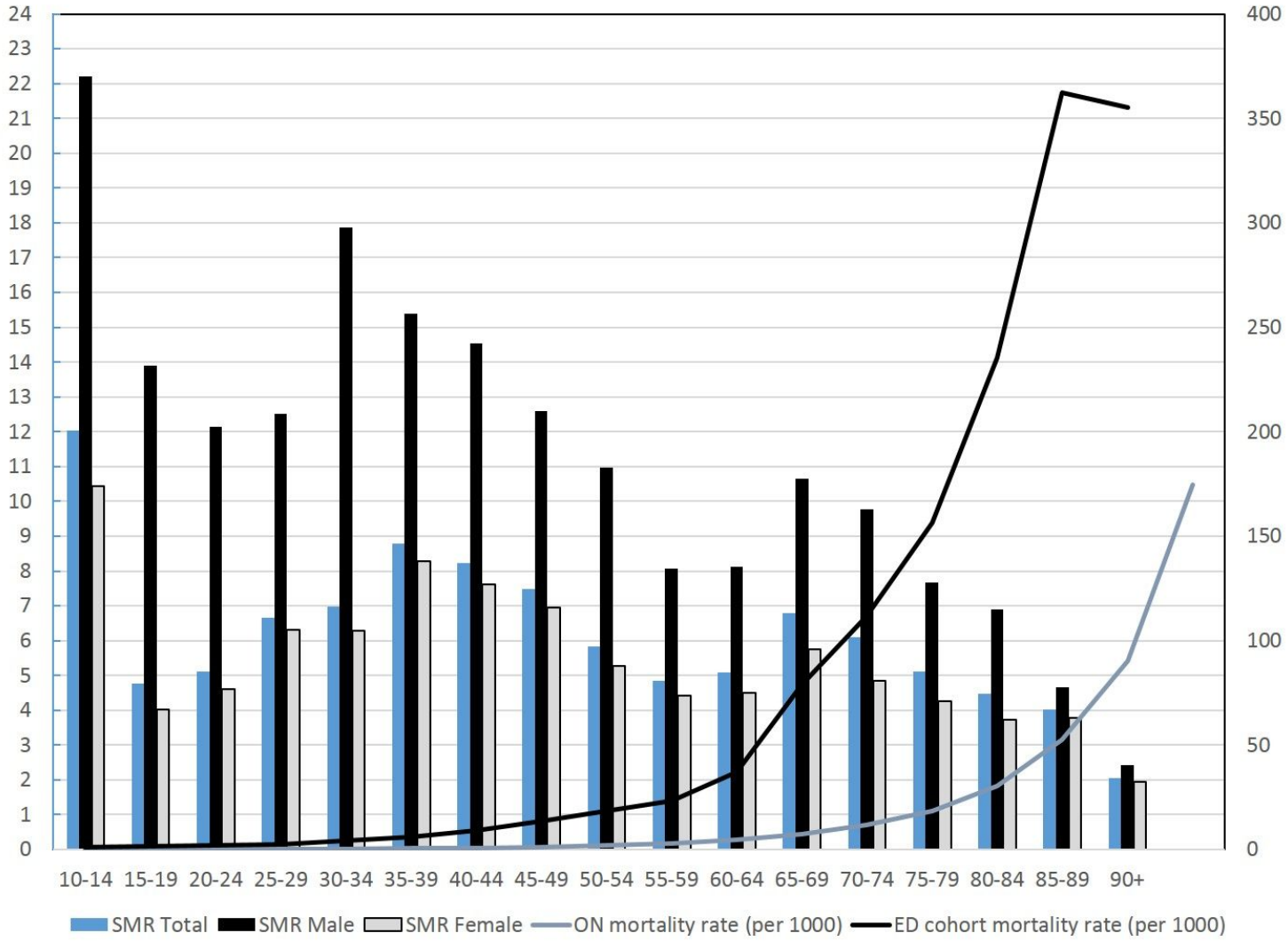
Legend: COPD- Chronic Obstructive Pulmonary Disease; HIV, Human Immuno-Deficiency Virus

Appendix Table 1: Age-Sex matched person years of life lost and 95% CI in ED cohort and Ontario population in 2011

	ED Cohort PYLL (95% CI)	Ontario Population PYLL (95% CI)	Excess PYLL (%)
Both Sexes	191.5 (189.3-193.7)	29.6 (28.8-30.5)	85%
Male	375.4 (364.4-386.6)	29.6 (28.7-30.5)	92%
Female	174.8 (172.6-177.0)	29.7 (26.6-32.7)	83%

Legend: ED – eating disorders; CI – confidence interval; PYLL – Person Years of Life Lost

Figure 1: Standardized mortality ratios-by sex and age-group, all-cause mortality rates observed within the eating disorders cohort (1991-2013) and Ontario (2011) mortality rates



Y1 axis label (left) Standardized Mortality Ratio (SMR)
Y2 axis label (right) Observed morality rate (per 1000 person years)